UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,378	02/27/2004	Shui-on Leung	018733-1359	7939

22428 7590 01/12/2006

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
BRISTOL, LYNN ANNE	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/787,378	LEUNG ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-15 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-15 are under examination.

Sequence Compliance

2. The primers discussed in paragraphs 0149-0151 of the specification are not defined by Sequence Identifiers from the Sequence Listing. Appropriate correction is required.

Specification

3. The disclosure is objected to because of the following informalities: The first line of the specification should be updated to indicate that application 09/894,839 is now abandoned and that application 09/155,107 is now U.S. Patent 6,254,868.

4. It is noted that Applicants' have introduced several amendments to the specification and drawings of the originally filed provisional application (60/013,709) at the time of filing the PCT application (PCT/US97/04196). Wherein the PCT application, the 371 application, 09/155,107, and subsequent child applications (09/155,107, 09/894,839 and 10/787,378) appear to be a C-I-P of the provisional application, none of these amendments were introduced by preliminary amendment nor mentioned in the Oath/Declaration filed at National Stage entry for 09/155,107. In brief, these amendments are the following.

Example 11 of 60/013,709 has been amended to substitute Figure 12 for Table 1. Notably, original Table 1 did not mention the antibodies hLL2HCN3-HCN5 or their glycosylation properties. Also, the text at p. 47, lines 23-48 has been deleted, referring to the final expression constructs for the heavy chain glycosylations. Finally, section 2

(page 48, line 8 thru page 51, line 36) has been replaced by paragraphs 0155-0158. The original section 2 discussed the details of constructing the hLL2HCN1 and hLL2HCN2 antibodies and their migration patterns on SDS-PAGE following enzymatic N-deglycosylation. Paragraphs 0155-0158 now discuss the comparison of N-glycosylation for hLL2HCN1 and hLL2HCN5.

Finally, the 60/013,709 specification did not contain Examples 12 and 13 as filed in PCT/US97/04196.

Figure 1A of 60/013,709 was amended to insert the sequence for REI FRs.

Figure 3B of 60/013,709 was amended to change the BglII enzyme restriction site to a BstEII enzyme restriction site in the VHpB5 vector.

Figures 4A, 4B and 5A of 60/013,709 were amended to change the CDR3 domain as to encompass one less amino acid.

Finally, the 60/013,709 application did not contain Figure 12 as filed in PCT/US97/04196.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 at lines 8 and 11 is indefinite for reciting "in the CH1 region gene" as it is unclear which of the two genes is being engineered with a mutation.

b. Claim 1 at line 8 is indefinite for reciting "and operably linked to expression control elements" because it is unclear whether the engineered genes for the heavy and light chains are linked to those elements or only those portions of the genes where a mutation for glycosylation has been engineered into the respective gene.

c. Claims 7-9 are indefinite for reciting "glycosylation is located on a site...of Figure 12" for Claim 7, "glycosylation site...of Figure 12" for Claim 8 and "glycosylation site...of Figure 12" for Claim 9 as the meaning is unclear. It is unclear if the phrase in the claims is meant to be directed to the sites represented in bold letters or to the entire amino acid sequence listed in Figure 12.

d. Claim 8 is indefinite for reciting "the HCN5 site (SEQ ID NO: 10)" as the specification (p. 8, paragraph 0038), Figure 12 and the Sequence Listing (SEQ ID NO: 14), taken together, teach that HCN5 corresponds to SEQ ID NO: 14.

e. Claim 10 is indefinite for reciting "specificity of the hLL2 antibody" as it is unclear if the phrase means binding specificity (i.e., is B-cell specific) or affinity.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The claims 3, 10 and 12-13 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are 1) known and readily available to the public; 2) reproducible from the written description.

a. hLL2 antibody hybridoma (Claims 10-12)

1) It is unclear if a cell line, which produces an antibody having the exact chemical identity of hLL2, is known and publicly available, or can be reproducibly isolated without undue experimentation. The specification identifies the source of the LL2 hybridoma cells (p. 11, paragraph 0046) but a search of public databases does not show that a deposit or commercial cell line is publicly available. Furthermore, there is no indication in the specification that the humanized LL2 antibody as claimed is readily available to the public, and the specification does not provide sufficient guidance or direction to assist one skilled in the art to make and/or use the hLL2 to which glycosylation sites were introduced. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

b. For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with

very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species hLL2. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

b. pdHL2/dhfr expression vector (Claims 3 and 13)

1) It is unclear if an expression vector, having the exact chemical identity of the pdHL2 vector comprising the amplifiable gene dhfr, is known and publicly available, or can be reproducibly isolated without undue experimentation. It is noted that a bacterial strain containing a linear plasmid, pDHL2, has been deposited with the ATCC (ATCC # 90624), but there is no indication that a pDHL2 vector isolate containing the dhfr gene is publicly available. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above vector, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (a) the claimed vector; (b) a bacterial cell line which produces the chemically and functionally distinct vector claimed; and/or (c) the claimed vectors nucleic acid sequence is an unpredictable event.

2) The specification lacks deposit information for the deposit of the pdHL2/dhfr vector. With respect to the pdHL2/dhfr vector, there is no indication in the specification that the vector is readily available to the public and the specification does not provide

that the vector is readily available to the public and the specification does not provide any guidance or direction to assist one skilled in the art to make and/or use this vector. Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed vectors or cell lines reproducing the claimed vectors, a suitable deposit is required for patent purposes, evidence of public availability of the claimed vectors or cell lines reproducing the claimed vectors or evidence of the reproducibility without undue experimentation of the claimed vectors, is required.

If the deposit for the hLL2 antibody hybridoma or the pdHL2/dhfr expression vector is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or

assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession

at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

8. Claims 1-6 and 10-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making (a) an antibody comprising a N-linked glycosylation site specified in SEQ ID NO:10-14 of the human CH1 domain and (b) an antibody comprising SEQ ID NO: 10 and 14 wherein the antibody is glycosylated, does not reasonably provide enablement for making antibodies which are glycosylated at O-linked sites, any antibodies which comprise CH1 O- or N-linked sites except the exemplified N-linked glycosylated antibodies expressed in myeloma Sp2/0-Ag14 cells, or antibodies glycosylated at any Ck region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability of the art, the breadth of the claims, the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to producing antibodies or antibody fragments which are engineered to contain an N-linked or O-linked glycosylation site at any position in the constant light chain region and the antibodies are specific for any B-cell or B-cell antigen.

The specification teaches the LL2 is a highly specific anti-B-cell lymphoma and anti-lymphocytic leukemia cell murine monoclonal antibody (see page 2, 005).
The specification teaches humanization of the LL2 antibody (see Figure 1). The specification teaches hLL2HCN1 and hLL2HCN5 are N-linked glycosylated in the CH1 domain (see pages 41-42, 0155-0159) and that mutants that were designed to contain a glycosylation site in the constant light chain region (KCN1-4) were "either not glycosylated at all, or glycosylated at an insignificant level." (see page 42, 0155) or "not found to be glycosylated." (See page 43, 0157). The specification teaches conjugation of aminobenzyl DTPA and dextran-doxorubicin to the hLL2HCN1 and hLL2HCN5 antibody and the F(ab')2 of said antibodies (see page 43, example 12).
The specification fails to teach monoclonal antibodies engineered to contain a N- or O-linked glycosylation site which is glycosylated at any other position than the N-linked sites described above for the hLL2 antibody in the CH1 domain. The specification does not describe adding a glycosylation site to any antibody in the constant light chain.
The claims broadly encompass mutations, which introduce a N- or O-linked glycosylation site anywhere in the constant light chain region. The claims also broadly encompass antibodies that contain a glycosylation site but wherein the antibody is not actually glycosylated. It is known that not all cells glycosylate the same. As evidenced

by Wright et al (Springer Semin Immunopathology ,15 :259-273 (1993)), the glycosylation of the Vh chain "contributes to alterations in protein stability, leading to the formation of immune complexes or tissue deposition" and Wright et al further caution that "disruption in the regulation of glycosylation can lead to the expression of altered carbohydrate structure (such as galactosyl sugars) with a resulting glycoprotein exhibit properties (such as a tendency towards aggregation) that contribute to disease" (page 270, second to last paragraph). Moreover Wright. et al teach while N-linked glycosylation is a wide spread post translational modification, occurring among mammalian, yeast, insect and plant cells, "the processing steps in the Golgi apparatus vary among cell types". (Page 259, second paragraph). Wright documents that plant cells use xylose, mammalian cells use sialic acid, and yeast add many mannose monomers than mammalian cells. Also insect cells do not appear to process the carbohydrates beyond the Man3 GLC Nac2 step. Accordingly, one skilled in the art would reasonably conclude that the tertiary structure of glycosylated antibodies, if actually glycosylated, which are encompassed by the broadly written claims would differ, based upon the teachings of Wright et al.

Further, Wright et al specifically teach that "the position of the carbohydrate addition appears to influence the structure of the added carbohydrate" (page 269, first full paragraph) and that "glycosylation can induce structural abnormalities in the light chain that lead to tissue deposition" (page 266-267, bridging paragraph). Further, Wright et al go on to teach that "many Vh3 genes ... contain potential N-linked glycosylation sites as ASN 72, in FR3, although it has not yet been determined whether

any of these sites are in fact glycosylated". Finally, Wright et al teach that the sugars may fill "pockets" within the immunoglobulin , thus one of ordinary skill in the art would reasonably conclude that addition of carbohydrates to an antibody would alter the tertiary structure as evidenced from Delente (Trends in Biotechnology 3, letters to editor, No.9, (1985)) which teaches each glycosylated protein must be evaluated individually to determine the importance of glycosylation to its function and stability. Thus Wright et al teach the unpredictability of adding a glycosylation site to an antibody molecule, specifically that some additions result in protein aggregation that the position of the addition is important for determining whether the glycosylation site is in fact recognized by the cell, and once glycosylated, whether the antibody is more or less stable and binds antigen like the unaltered form. One skilled in the art would also reasonably conclude from Wright et al that glycosylation in the CH1 or constant K (CK) region could have similar structural effects as those in the light chain mentioned above. Moreover, the specification teaches that sites at KCN1-4 were not glycosylated (see page 43, 0157).

As evidenced by Olden et al (Biochem et Biophys Acta 650:209-232 (1982)), carbohydrate structures are a form of sorting signals used by the cells and that O-linked glycosylation differ from N-linked glycosylation due to the sugars which are added to each type during protein processing. O-linked carbohydrates use galNAC while N-linked carbohydrates use GlcNAC (see page 225, second column, first paragraph). Olden teaches that O-linked carbohydrates differ in tertiary structure from N-linked carbohydrates and therefore, one skilled in the art would reasonably conclude that

antibodies possessing O-linked sugars would also differ in their tertiary structure from those antibodies expressing N-linked sugars.

Moreover, while the N-linked carbohydrate addition site is specifically the sequence "ASP-X-SER/THR, where X may stand for any amino acid, the O-linked addition site is less defined as only a serine or a threonine residue. Carbohydrate moieties are not attached to all lumenal serine or threonine residues and it would be unpredictable to determine at which lumenal positions a serine or a threonine could be placed within the antibody molecule so that the serine or threonine would be glycosylated. Once glycosylated, whether by the N-linked or O-linked mechanism, it would require undue experimentation to determine whether the antibody expression, stability, tertiary structure or affinity had been affected.

Since the state of the art of protein modification suggests that the effects of sequence alterations are unpredictable, and furthermore, as evidenced by Wright et al, Delente, and Olden et al concerning the unpredictability of adding carbohydrates to proteins and since the specification provides inadequate guidance as to which changes would result in a functional antibody, wherein the glycosylation site is actually used, and the antibody stability/function is not reduced, undue experimentation would be required to determine which addition sites would result in the glycosylated antibody molecule that could still be expressed in a soluble form from a eukaryotic host and bind its antigen.

Therefore, in view of the lack of guidance in the specification and in view of the unpredictability in the art of glycosylation of proteins as evidenced by Wright et al, Olden et al, and Delente and the unpredictability of glycosylation of antibodies as evidenced by

the specification, one of skill in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 4-6, 10-11 and 14-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of US Patent No. 6,254,868 (hereinafter referred to as the "'868 patent") in view of Hansen et al. (U.S. Patent 5,635,603, filed 12/5/94; hereinafter referred to as "Hansen"). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the patent in combination with the reference render the instant claims obvious.

Claims 1, 4-6, 10-11 and 14-15 recite a method for producing an antibody containing glycosylation sites engineered into the DNA for a CH1 region of a heavy chain gene and the DNA for a constant light chain gene, where the genes are cloned into an expression vector and expressed in a glycosylation-permissive cell for production of antibodies with the site-directed, glycosylated regions. The claims encompass an antibody having the binding properties of a humanized LL2 antibody.

Claim 9 of the '868 patent recites a method for producing an antibody containing glycosylation sites engineered into the DNA for a CH1 region of a heavy chain gene of an antibody, where the genes for a) heavy chain DNA engineered at the CH1 region with a glycosylation site and b) a constant light chain, are cloned into an expression vector, and expressed in a glycosylation-permissive cell for production of antibodies with the site-directed, glycosylated regions.

Claim 9 does not recite engineering a glycosylation site into the DNA for the constant light chain of the antibody, or cloning both the engineered heavy and light chain genes into an expression vector, nor does the claim encompass an antibody having the binding properties of a humanized LL2 antibody.

Hansen teach methods for making a humanized antibody, which contains an N-glycosylation site at alternative positions of the heavy and light chain (see generally, Col. 8, line 39 to Col. 13, line 32, specifically, Col. 10, lines 16-36). Hansen further teach that "a glycosylation site can be introduced into an immunoglobulin light chain by synthesizing a light chain gene with mutually priming oligonucleotides in which one of the oligonucleotides contains the desired mutation. Techniques for the construction of

large synthetic genes are well known to those in the art..." (Col. 9, lines 36-43). Hansen teach expressing the glycosylated antibody in SP2/0 myeloma cells (Col. 11, line 39). Finally Hansen teach a method for glycosylating amino acids 18-20 of the light chain for a humanized LL2 antibody, thus Hansen teaches a glycosylated antibody having the binding properties of a humanized LL2. Hansen also teaches the advantages of introducing glycosylation sites into antibodies (Abstract; Col. 22, line 30 to Col. 25, line 34).

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have created an antibody engineered at the CH1 of the heavy chain and constant light chain genes for producing glycosylated antibodies in view of Claim 9 of the '868 patent and Hansen, because Claim 9 recites and Hansen teach a method(s) of engineering of a CH1 heavy chain gene of an antibody and expressing the antibody in glycosylation-permissive cells to produce a glycosylated antibody. The general teaching of Hansen supports methods for glycosylating both heavy and light chain genes in view of the state of molecular cloning for large molecules such as antibodies, and specifically the glycosylation of LL2, as well as there being a long felt need to provide and improve antibody immunoconjugates for therapeutic and diagnostic purposes. Therefore, the invention of Claims 1, 4-6, 10-11 and 14-15 as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by Claim 9 of the '868 patent in view of the Hansen reference.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LAB

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER